AMENDMENTS TO THE DRAWINGS:

Please substitute the attached replacement, Figures 1-26, for the original drawings in the application. The replacement drawings do not introduce new matter.

REMARKS

These remarks are in response to the Office Action mailed March 2, 2006. The specification has been amended to incorporate essential matter from Appendix B of the application as filed. The added paragraphs are from Appendix B, which had been incorporated by reference when the application was originally filed. No new matter is believed to have been introduced.

I. IN THE SPECIFICATION

The title of the invention has been amended to be more clearly indicative of the invention to which the claims are directed, in accordance with the Examiner's suggestion.

The specification has been amended to incorporate essential matter from Appendix B of the application as originally filed. Applicants have deleted reference to Appendix A and B.

II. IN THE DRAWINGS

Two sets of drawings were submitted with the application as originally filed. Figures 1-15, as described in the application beginning at paragraph [0023] on page 5, and Figures 1-11, attached to Appendix B and as described in Appendix B beginning on line 20, page 10. Applicants have amended the page numbers of the two sets of drawings to be one set of drawings, Figures 1-26. Further, Applicants have incorporated the description of the Figures from Appendix B into the application.

III. OBJECTIONS TO THE CLAIMS

Claim 1 is objected to due to the incorrect spelling of "utereric", and the abbreviation "UB" in the second line of the claim. Applicants have amended the claim to correct the spelling error and to state the definition of the abbreviation the first time it appears, according to the suggestion of the Examiner.

Claim 2 is objected to due to the abbreviations "FGF1" and "GDNF". Applicants have amended the claim to state the definition of the abbreviation the first time it appears, as suggested by the Examiner.

Claim 3 is objected to due to the incorrect spelling of "produce". Applicants have amended the claim to correct the spelling error.

Claim 7 is objected to due to the term "proteoglycans" listed twice. Applicants have amended the claim to delete the second listing of "proteoglycans", as suggested by the Examiner.

Accordingly, the objections may be properly withdrawn.

IV. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 3-7 stand rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement. In particular, the Examiner alleges that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleges there is no evidence that the inventors were in possession of isolated active fragments of pleiotrophin and/or heregulin at the time of filing. Applicants respectfully traverse this rejection.

Applicants submit that pleitrophin is a known protein. The Examiner is directed to GenBank accession number:CAA37121, submitted May 2, 1990. Thus, pleiotrophin was known in the art at the time of filing of the application. It would not require undue experimentation for one of skill in the art to assay pleiotrophin. A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 3 USPQ2d 1737 (Fed. Cir. 1987); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann* Maschinenfabrik *GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art.

Section 112 requires the specification to be enabling only to a person "skilled in the art to which it pertains, or with which it is most nearly connected." In general, the pertinent art should be defined in terms of the problem to be solved rather than in terms of the technology area, industry, trade, etc. for which the invention is used.

Further, the Examiner alleges that there is insufficient written description provided in the disclosure to adequately describe the precise action GDNF and/or FGF1 have on the branching morphogenesis of ureteric bud cells, and without such a description, allegedly there is no evidence that the inventors were in possession of functional equivalents of homologues of GDNF and/or FGF1 at the time of filing. only heregulin. Applicants respectfully traverse.

GDNF and FGF1 are also well known in the art. Due to the length of these peptides, it would not require undue experimentation for one of skill in the art to obtain functional equivalents or homologues. As noted above, a patent need not teach, and preferably omits, what is well known in the art.

Claims 1-7 stand rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement. In particular, the Examiner alleges that while being enabling for a method of inducing ureteric bud cells to undergo branching morphogenesis in culture comprising culturing ureteric bud cells in either BSN-CM or pleiotrophin, it allegedly does not reasonably provide enablement for inducing UB cells to undergo branching morphogenesis in culture comprising only heregulin. The Examiner's attention is drawn to the last line of page 13, continuing to the first three lines of page 14, and Figs. 5 and 8 in the application. Here, Applicants describe the use of heregulin along with or as a substitute for pleiotrophin. As to working examples, Applicants respectfully submit that predictability in the art refers to the ability of one skilled in the art to extrapolate the disclosed results to the claimed invention. Applicants respectfully submit that one skilled in the art can readily anticipate the use of heregulin to provide similar

morphogenic growth-promoting ability on the UB cells. Accordingly, withdrawal of this rejection in proper and respectfully requested.

V. REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-7 stand rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner alleges that in claim 1 it is unclear what 'conditions' induce the UB to undergo branching morphogenesis. The Examiner further alleges that it is not clear what is considered a 'sufficient time' or 'sufficient conditions' so as to produce tubular branches in claim 3. Applicants respectfully traverse.

The specification describes "sufficient time and under sufficient conditions" to be that which allow the cells and the composition to interact, wherein the composition stimulates branching tubular morphogenesis, on page 3, paragraph [0013]. In determining definiteness in this matter, the proper test is whether or not one skilled in the art could determine specific values for the amount based on the disclosure. *See In re Mattison,* 509 F.2d 563, 184 USPQ 484 (CCPA 1975). For instance, the phrase "an effective amount . . . for growth stimulation" was held to be definite where the amount was not critical and those skilled in the art would be able to determine from the written disclosure, including the examples, what an effective amount is. *In re Halleck,* 422 F.2d 911, 164 USPQ 647 (CCPA 1970). Applicants respectfully submit that one skilled in the art can readily determine what is considered a sufficient time or sufficient conditions so as to produce tubular branches in claim 3, from the written disclosure as noted above. Accordingly, withdrawal of this rejection in proper and respectfully requested.

Further, the Examiner alleges there is insufficient antecedent basis for "the plurality of branch tips" in the 9th line of claim 3. Applicants have amended claim 3 to provide proper antecedent basis. Thus, withdrawal of this rejection is proper and respectfully requested.

The Examiner alleges that it is not clear in claims 4 and 5 which culture medium is to further comprise the GDNF or FGF1. To provide clarity, Applicants have amended claim 3 to recite one culture medium.

The Examiner alleges that in claims 6 and 7, it is not clear which biocompatible matrix is being referenced. To provide clarity, Applicants have amended claim 3 to recite one biocompatible matrix.

The Examiner further alleges that in claim 6, collagen is one of the listed biocompatible matrix materials; however claim 7 also requires collagen to be one of the materials added to the matrix material. Applicants respectfully traverse. Claim 7 lists types of collagen thereby providing limitations to claim 6.

Accordingly, withdrawal of this rejection in proper and respectfully requested.

VI. REJECTION UNDER 35 U.S.C. §103

Claims 1, 3, 6 and 7 stand rejected under 35 U.S.C. §103, as allegedly unpatentable over Sakurai et al. (PNAS, 1997), in view of "Basic Techniques for Mammalian Cell Tissue Culture" (Current Protocols in Cell Biology, 1998), Naughton et al. (US 2003/0007954), and "Overview of Extracellular Matrix" (Current Protocols in Cell Biology, 1998). Applicants respectfully traverse this rejection.

Applicants respectfully submit that the Examiner is using hindsight to arrive at the claimed invention. For example, the Office Action alleges that it would have been obvious to arrive at Applicants' invention based upon the reading of Sakurai et al. because it would have been " well within the purview of one of ordinary skill in the art" as part of routine animal cell tissue culture methods, to divide and resuspend subpopulations of the UB cells. Applicants submit that with such global knowledge imputed to one of skill in the art it would be obvious in hindsight to arrive at almost any invention with the mere motivation of continually subculture the growing of cell tissue culture of a species because the genus cell tissue culture techniques are well known in the art. As recognized by the Examiner the methods and Sakurai et al. are different than those presently claimed (see, e.g., page 16).

In order to overcome this deficiency, the Examiner appears to combine Sakurai et al. with "Basic Techniques for Mammalian Cell Tissue Culture" (Current Protocols in Cell Biology, 1998), Naughton et al. (US 2003/0007954), and "Overview

of Extracellular Matrix" (Current Protocols in Cell Biology, 1998). "Basic Techniques for Mammalian Cell Tissue Culture" (Current Protocols in Cell Biology, 1998), Naughton et al. (US 2003/0007954), and "Overview of Extracellular Matrix" (Current Protocols in Cell Biology, 1998) do not teach or suggest the biocompatible matrix of the invention, nor do they add anything to the teachings of Sakurai et al. Sakurai et al. teaches and suggests that GDNF has very limited morphogenic ability compared to other growth factors. In fact, one of skill in the art would recognize upon reading Sakurai et al. in view of "Basic Techniques for Mammalian Cell Tissue Culture" (Current Protocols in Cell Biology, 1998), Naughton et al. (US 2003/0007954), and "Overview of Extracellular Matrix" (Current Protocols in Cell Biology, 1998). "Basic Techniques for Mammalian Cell Tissue Culture" (Current Protocols in Cell Biology, 1998), Naughton et al. (US 2003/0007954), and "Overview of Extracellular Matrix" (Current Protocols in Cell Biology, 1998) that GDNF is a poor morphogenic factor (see, FIG. 5). Applicants submit that the data presented in Sakurai et al. clearly demonstrate that other factors (e.g., IGF, FGF) have far better UB morphogenic effects than GDNF. Accordingly, one of skill in the art would not have been motivated to combine GDNF with BSN-CM as recited in the present claims. In fact, Sakurai et al. actually teaches away from the use of GDNF because of its poor morphogenic effects on UB cells.

Applicants submit that the there is no motivation to combine the references to arrive at Applicants' invention. Applicants submit that Sakurai et al. actually teaches away from Applicants' invention. The motivation to arrive at Applicants' invention can only be found in hindsight reconstruction particularly where, as the case is here, the teachings clearly indicate that GDNF is a poor morphogenic factor. For at least the foregoing reasons, Applicants submit that Applicants invention is non-obvious over the cited references. Accordingly, Applicants respectfully request withdrawal of the rejection.

VII. OBVIOUSNESS TYPE DOUBLE PATENTING

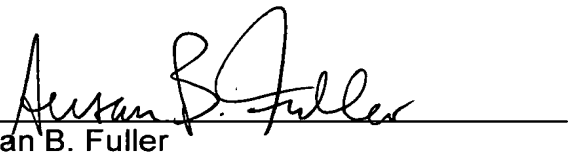
Claim 1 stands provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claim 1 in copending application no. 09/595,195. Applicants submit herewith a Terminal Disclaimer. The Terminal Disclaimer obviates this rejection. Accordingly, Applicants respectfully request withdrawal of this rejection.

No fee is believed to be due with respect to the filing of the present response. However, the Commission is authorized to charge any required fee, or credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL PC

Date: April 6, 2006

By: 
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